

REMARKS

Claims 11, 14, 21-25 and 27-32 are presently pending. In view of the arguments set forth below, Applicants respectfully submit that claims 11, 14, 21-25, and 27-32 are in condition for allowance.

Interview Summary

Applicants thank the Examiner for the courtesy of the telephonic interview on May 1, 2008, during which the following outstanding obviousness rejections and related references cited by the Examiner were discussed.

Rejection of Claims 11, 14, 21-25 and 27-32 Under 35 U.S.C. § 103(a)

I.) The Examiner has rejected claims 11, 14, 21-25 and 27-32 under 35 U.S.C. § 103(a) as being unpatentable over Mantius *et al.* (U.S. Patent No.: 5,320,861), Zafriri *et al.* (Antimicrobial Agents and Chemotherapy (1989) 33(1):92-98) and Sperti *et al.* (U.S. Patent No.: 4,477,361). Specifically, the Examiner asserts that:

Mantius teaches a cranberry juice product that is defined by applicant as the Tomah presscake. Mantius does not teach enriching this product in cinnamic acids. However, Zafriri teaches that cranberry juice is an antibacterial agent against *Escherichia coli*. An artisan of ordinary skill would then reasonably expect that the cranberry juice of Mantius would also function as antibacterial agent [sic] against *E. coli*. This reasonable expectation of success would motivate the artisan to use the Tomah presscake of Mantius to treat *E. coli* infection. Sperti teaches that cinnamic acid is an antibacterial agent against *Escherichia coli*...Based on the disclosure by these references that these substances are used in antibacterial compositions against *E. coli*, an artisan of ordinary skill would have a reasonable expectation that a combination of the substances would also be useful in creating a single antibacterial composition against *E. coli*. Therefore, the artisan would have been motivated to combine the claimed ingredients into a single composition" (pages 2-3 of the present Office Action).

Applicants respectfully traverse this rejection. In sum, as discussed in more detail below, the primary reference of Mantius teaches a Tomah presscake which is not enhanced or enriched for cinnamic acid. The secondary reference of Zafriri teaches that *fructose* added to cranberry juice has antibacterial activity against *E. coli*. The third reference of Sperti merely teaches that cinnamic compounds form a protective, antibacterial film when applied as surfactants added to non-edible products, *e.g.*, soaps and detergents. Accordingly, one of ordinary skill in the art

would **not** have been motivated to have combined these references in the manner suggested by the Examiner to result in a Tomah presscake enriched for cinnamic acid, as there is no nexus whatsoever among the references, and no reason to have applied them in this manner.

Specifically, as an initial matter, Applicants note that the Tomah presscake taught by Mantius is not a *cranberry juice*, as indicated by the Examiner. In fact, Applicants' specification teaches that decharacterized fruit, such as the Tomah presscake, is fruit **from which the juice has been extracted** (see, for example, page 6, lines 1-5 of the specification). Accordingly, the Tomah presscake of Mantius is not a cranberry juice product.

Zafriri teaches that cranberry juice cocktail inhibits adherence of *E. coli* to yeast and mammalian cells. However, Zafriri teaches that this antibacterial activity is **due to fructose added** to the cranberry juice cocktail. Specifically, Zafriri teaches that cranberry juice cocktail is a 25% dilution of native cranberry juice to which glucose and fructose have been added to concentrations of about 7 and 5%, respectively (see Zafriri *et al.*, page 92, column 2, lines 10-13). Zafriri further teaches that the inhibition of adherence of type-1 fimbriated *E. coli* to yeast cells **is largely due to the addition of fructose** to the cranberry juice cocktail, as "the inhibitory activities of dilutions of 5% fructose were similar to those of the same dilutions of the [cranberry juice] cocktail for each of the three strains of *E. coli* tested" (see Zafriri *et al.*, page 94, column 2, paragraph 1, line 12, to page 95, column 1, paragraph 1, line 2). Indeed, Zafriri concludes that "[t]aken together, our data show that most or all of the inhibition of yeast aggregation by the cocktail or juice is due to the fructose content" (see Zafriri *et al.*, page 96, column 2, paragraph 3, lines 10-12). With respect to mammalian cells, Zafriri likewise teaches that "[t]he adherence of *E. coli* 346 to Chinese hamster ovary cells and to mouse adrenal cells was inhibited similarly by dilutions of cranberry juice cocktail and by fructose at corresponding concentrations" (see Zafriri *et al.*, page 95, column 1, paragraph 2, lines 2-5). Accordingly, Zafriri provides motivation to enrich cranberry products for **fructose**, not cinnamic acid as claimed.

Sperti merely teaches that cinnamic compounds are useful when combined with surfactants in non-edible products, including soaps and detergents. The authors teach that these compounds have antibacterial activity and, when incorporated into superfatted soaps, form a

protective film on the washed surface, *e.g.*, the skin (see Sperti *et al.*, column 1, lines 49-55 and column 4, lines 8-12).

Based on the above, a person of ordinary skill in the art would *not* have been motivated to have added cinnamic acid to an edible product, such as the Tomah presscake of Mantius, to treat *E. coli* infection. Notwithstanding that Zafriri teaches that *fructose*, not cinnamic acid, is the antibacterial component of cranberry juice, one of ordinary skill would not have applied this reference to the teachings of Mantius, since the Tomah presscake represents fruit *from which the juice has been extracted*. Furthermore, as Zafriri teaches that the reduction in adherence of type-1 fimbriated *E. coli* observed following treatment with a cranberry juice cocktail was largely due to the *fructose* with which the cranberry juice had been supplemented, a person of skill in the art would not look to the components (*e.g.*, cinnamic acid) of cranberry products including the Tomah presscake for the inhibition of *E. coli*. Accordingly, one of ordinary skill in the art would not have been motivated to have combined the Tomah presscake taught by Mantius with the surfactant cinnamic compounds taught by Sperti. This lack of motivation only would have been increased by the fact that Sperti teaches formulating cinnamic compounds as *soaps and detergents*, not as food products which are *suitable for administering to a subject*, as required by the claims. Accordingly, the presently claimed cranberry extract enriched for cinnamic acid, wherein the cinnamic acid is present in a greater amount than that found in a cranberry Tomah presscake, would not have been obvious in view of the teachings of Mantius in combination with Zafriri and Sperti.

II.) The Examiner additionally rejects claims 11, 14, 21-25 and 27-32 under 35 U.S.C. § 103(a) as being unpatentable over Mantius *et al.* (U.S. Patent No.: 5,320,861), Marwan *et al.* (J. Food Sci. (1982) 47:774-778), and Liu *et al.* (Int. J. Cancer (1995) 62:345-350). Specifically, the Examiner maintains that:

Mantius teaches the cranberry product, the Tomah presscake. Mantius does not teach enriching the Tomah presscake for cinnamic acid. Marwan teaches that cinnamic acid is present in cranberries. Thus, an artisan of ordinary skill would reasonably expect that the Tomah presscake of Mantius would contain cinnamic acid. Liu teaches that cinnamic acid is useful in treating a variety of cancers. The artisan would also reasonably expect that it would be beneficial to increase the concentration of cinnamic acid in this product based on the teaching of Liu that cinnamic acid is useful in treating cancer. Therefore, an artisan of ordinary skill would be motivated to modify the Tomah presscake of Mantius

to enrich the presscake for cinnamic acids based on the teaching by Liu that cinnamic acids are beneficial compounds. (Office Action, page 4)

Applicants respectfully traverse this rejection. Applicants note initially that Marwan teaches that the following *hydroxycinnamic acid derivatives* are present in cranberries: 4-O- β -(glucosyl)_n-caffeooyl- β -glucose)_n; 3, 4- β -O-di-(glucosyl)_n-caffeooyl- β -(glucose)_n; β -O-(glucosyl)_n-p-coumaric acid; a phenolic acid-glucose ether; β -O-(glucosyl)_n-p-coumaroyl- β -(glucose)_n; p-coumaroyl- β -glucose; β -O-(glucosyl)_n-feruloyl- β -(glucose)_n; sinapoyl- β -(glucose)_n; and p-coumaric acid (see Marwan, page 776, Table 1). In contrast to the Examiner's assertion, *Marwan does not teach that cinnamic acid (i.e., (E)-3-phenylprop-2-enoic acid) is present in cranberries*. Indeed, Marawn isolated and identified numerous compounds from cranberries, but *did not* find cinnamic acid to be among the isolated compounds.

Accordingly, Mantius, the primary reference, teaches a Tomah presscake which is not enhanced or enriched for cinnamic acid. The secondary reference of Marwan merely teaches components of cranberries which *do not include* cinnamic acid. The third reference of Liu merely teaches that *in vitro* exposure of tumor cell lines to cinnamic acid resulted in growth arrest and induced differentiation. Therefore, based on the teachings of the cited references, one of ordinary skill in the art would not have had any more motivation to have combined the cinnamic acid of Liu with the Tomah presscake of Mantius, *than to have combined (i.e., supplemented) any other food product with cinnamic acid* to derive the beneficial effects thereof. Moreover, while Mantius and Marwan fail to teach or suggest that cranberries even contain cinnamic acid and Liu fails to teach or suggest that cinnamic acid induces growth arrest in tumor cells when incorporated as a component of a *food product*, even if a person of skill in the art had been motivated to supplement a food product with cinnamic acid, he or she would have logically chosen to enrich the countless number of food products that *lack* cinnamic acid in order to instill them with the beneficial compound, rather than to further supplement a product which *already* contains cinnamic acid. Accordingly, there would *not* have been any motivation for one of skill in the art to combine the teachings of Mantius, Marwan and Liu to yield a cranberry extract enriched for cinnamic acid, wherein the cinnamic acid is present in a greater amount than that found in a cranberry Tomah presscake, as required by the pending claims.

For the foregoing reasons, the claimed compositions are non-obvious over the teachings of Mantius, Marwan and Liu, either alone or in combination. Accordingly, Applicants respectfully request that the rejection of claims 11, 14, 21-25 and 27-32 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

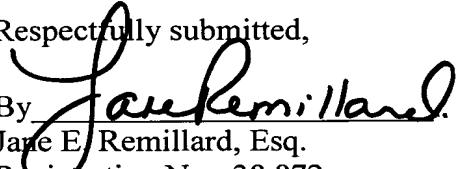
CONCLUSION

In view of the foregoing amendments and remarks, reconsideration and withdrawal of all rejections and allowance of all pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Dated: May 19, 2008

Respectfully submitted,

By


Jane E. Remillard, Esq.
Registration No.: 38,872
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant